REMARKS

Claims 80-92 are pending in the application. Claims 80-84 have been withdrawn from consideration as being directed to a non-elected invention. Accordingly, claims 85-92 are under examination in the above-identified application. Applicant has reviewed the rejections set forth in the Office Action mailed May 19, 2004, and respectfully traverse all grounds for the reasons that follow.

Claims 85-92 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite allegedly for reciting the terms "enhanced antibody" and "functional fragments thereof." The Examiner asserts that these terms encompass different forms and modifications and that it is not clear what particular enhancement or functional attribute is referenced by these terms.

Applicant submits that the terms are clear and definite as they are used in the claims. For example, the application teaches at page 16, lines 17-24, that functional fragments of an antibody can include antibody functional fragments such as Fab, $F(ab)_2$, Fv, single chain Fv (scFv). The application further teaches that other functional fragments can include, for example, heavy or light chain polypeptides, variable region polypeptides or CDR polypeptides or portions thereof so long as such functional fragments retain binding activity, specificity or inhibitory activity. *Id.* Similarly, the application also teaches, for example, at page 17, lines 3-6, the meaning of the term "enhanced" when used in reference to an antibody. Accordingly, the terms are sufficiently clear to set forth and claim the subject matter Applicant regards as the invention. Therefore, these grounds of rejection are respectfully requested to be withdrawn.

Claims 85-92 also stand rejected for indefiniteness for reciting the term "modifying" allegedly because it is a relative term and because the specification fails to provide a standard for ascertaining the direction, degree or endpoint of the modification.

Applicant submits that the objected term is clear and definite as it is used in the claims. The term "modify" or "modifying" has an ordinary and plain meaning which applicant has not deviated from. Moreover, the application teaches throughout various modifications or changes to a parent antibody, or functional fragment thereof, that exemplify a modification as the term is

used in the claims. Accordingly, the term is sufficiently clear and definite to set forth and claim the subject matter Applicant regards as the invention.

Claim 92 stands further rejected under 35 U.S.C. § 112, second paragraph, as indefinite for reciting the term "grafted antibody" allegedly because this term encompasses a number of recombinant forms of antibodies.

Applicant submits that the term is clear and definite as it is used in the claims. The application teaches, for example, at page 11, lines 19-24, that a grafted antibody refers to an antibody heavy or light chain, or functional fragment thereof, having substantially the same heavy or light chain CDR of a donor antibody. Accordingly, the term is sufficiently clear to set forth and claim the subject matter Applicant regards as the invention. Therefore, this ground of rejection is respectfully requested to be withdrawn.

Claim 85 stands rejected for indefiniteness allegedly for lacking antecedent basis for use of the term "the rate." Applicant has amended the claim 85 to correct this informality. Accordingly, this ground of rejection is moot and is respectfully requested to be withdrawn.

Claims 85-87, 90 and 91 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Schier et al. Further, claims 85-89 and 92 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Deng et al. Claims 85-89 and 92 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Marks et al., U.S. Patent No. 5,997,322, and claims 85-87 similarly stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Yelton et al.

Applicant claims a method for producing an enhanced antibody, or functional fragment thereof. The method includes modifying a parent antibody, or functional fragment thereof; obtaining one or more variant antibodies, or functional fragments thereof, having one or more amino acid substitutions in one or more variable regions compared to the parent antibody, and measuring an association rate constant (k_{on}) of the one or more variant antibodies, or functional fragments thereof, to an antigen, wherein a variant antibody, or functional fragment thereof, having an association rate to an antigen that is 4-fold higher or greater compared to the rate of the parent antibody binding to the antigen is an enhanced antibody, or functional fragment thereof.

In each of the above rejections, the Office appears to equate an increase in association rate (K_a) with an increase in association rate (k_{on}). However, the two parameters differ. In contrast to the apparent assertions in the Office Action, none of the cited art teach the invention as claimed, wherein an association rate constant (k_{on}) is measured or wherein a variant antibody is produced that has a 4-fold higher or greater association rate (k_{on}) compared to the association rate of a parent antibody. Accordingly, none of the cited art anticipate the claimed invention and withdrawal of these grounds of rejection is respectfully requested.

Claims 85-92 also stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Schier et al. in view of Foote et al. Schier et al. is alleged to describe a method of mutating CDR3 regions to produce antibody variable region heavy and light chains that exhibit picomolar affinity. Foote et al. is alleged to describe a method of reshaping or grafting an antibody that generates mouse CDRs inserted into a human antibody framework. The Office asserts that it would have been obvious to obtain a method of humanization and affinity maturation of an antibody by randomizing CDR and framework residues because Schier et al. describe a method of achieving picomolar affinities through mutation of CDR3 and Foote et al. describe substitutions in framework regions.

As set forth above, Schier et al. appears to describe methods of producing an antibody having a higher K_a. Schier et al. does not appear to teach or suggest a method of producing an antibody having a higher k_{on}. Nor does Schier et al. teach or suggest producing a variant antibody having a 4-fold higher or greater association rate (k_{on}) compared to the association rate of a parent antibody. Foote et al. is cited for allegedly describing antibody reshaping methods having apparent clinical applications. Therefore, Foote et al. does not cure the deficiencies of the primary reference. Because Schier et al. is directed to affinity, rather than association rate, and because Foote et al. fails to provide the missing teaching, suggestion or motivation, the cited combination of art fails to render obvious the claimed invention. Applicant therefore respectfully requests that this ground of rejection be withdrawn.

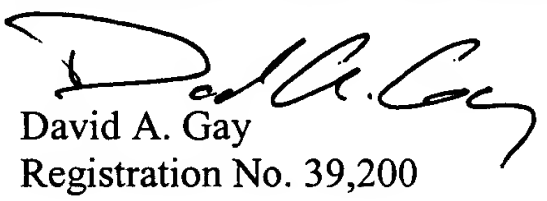
CONCLUSION

In light of the Amendment and Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



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Date: November 19, 2004

SDO 22167-1.066797.0109